

## REMARKS

Claims 1 through 29 continue to be in the case.

New claim 30 is being submitted. New claim 30 is based on the language of claim 5.

The Office Action refers to Claim Rejections - 35 USC § 102.

14. Claims 1-21 stand rejected under 35 U.S.C. 102(a) as being anticipated by Chamberlain (WO 93/01843).

Chamberlain according to the Office Action discloses a cardiovascular prosthesis with an initial sub-confluent seeding of endothelial cells on the surface thereof then forming a confluent monolayer of endothelial cells, with all the elements of claim 1. See page 11, lines 1-13 and abstract.

The endothelial cells of the present Invention have a particular cell density and exhibit a particular pattern relative to the printed Patent document WO 93/01843 to Chamberlain. According to the present Invention, the initial cell density amounts to 30 -- 50 percent in a homogeneous distribution, and the final cell density amounts to in fact 100 percent, and in fact prior to and after implantation, that is therefore surface

covering in contrast to the reference printed Patent document WO 93/018437, page 8, line 13. Since the cells are already in vitro, that is in the perfusion circulation, adapted to the flow conditions prevailing in vivo, that is in the blood vessel, no further cells disengage after implantation of the prothesis into the blood circulation according to the present invention. Based on sub confluent initial cell seeding and based on the growth to confluence under shearing forces rising up to physiological values, the cells exhibit a clearly stronger adherence, which stronger adherence conveys unique properties to the product obtained by the Invention method, that is the stable adhesion of the cells on the surface of the prothesis.

A cardiovascular prothesis defines an artificially produced body member frequently employed as a substitute for a lacking or defect body member, but also as an additional body member, as required by medical indication and limited by the adjective "" cardiovascular"" to the heart region and the blood vessel region. The term " cardiovascular prothesis" for example covers all blood conductors as well as the immediate vessel substitution of arteries and veins and the blood conductors with the medical

indication such as AV-shunts, but also more complex body members such as a cardiac valve.

Applicant submits that the shearing forces substantially influence the growth of the cells according to the present invention. The shearing forces exert a decisive influence on the growth, in particular in the sense of a cell subdivision of the endothel cells. The important influence on the growth and the influence on the growth conveying valuable properties to the product concerns the functional change of the cells, amongst others the elongation and orientation of the cells along the engaging shearing forces and the formation of an improved adherence and in particular of the cell adhesion at the surface of the prothesis. Corresponding suggestions relating to the general influence of the shearing forces onto the endothel cells can be gathered from the literature.

Literature relating to the influence of the shearing forces on the functional state:

[1] Chieng S., Song Li, J. Shyy: Effects of mechanical forces on signal transduction and the gene expression in endothelial cells. Hypertension 1998, 31: 162 to 169

[2] Chapel, D., S. Varner et al. : Oscillatory shear stress stimulation adhesion molecule expression in cultured human endothelium. Circ. Res. 1998, 82: 532 -- 539

[3] Schnittler, H., B. Püschel, D. Drenkhahn: Role of cadherins and plakoglobin in inter endothelial adhesion under resting conditions and shear stress. Am. J. Physiol. 1997, 273 (heart Circ. Physiol.): H 2396 -- H 2405.

In contrast, the shearing forces recited in the reference Chamberlain have only a small value.

The Office Action continues that:

Claims 1-18 are written as product-by-process claims, and according to MPEP § 2113, these claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production, but on the product itself.

Applicants urge that the process of the present invention furnishes unique properties to the resulting product, which properties are clearly outside the scope of the Chamberlain reference.

Reconsideration of all outstanding rejections is respectfully requested.

Respectfully submitted,

Manrico Paulitschke et al.

By: *Horst M. Kasper*  
Horst M. Kasper, their attorney  
13 Forest Drive, Warren, N.J. 07059  
Tel.: (908)526-1717; Reg.No. 28, 559  
Attorney's Docket No.: WEH205

\*%PAMEND(WEH205A4(sn(rep-am

## **MARKED-UP VERSION OF THE AMENDED CLAIMS**

**(Version with marking to show changes made)**

30. (new) The method for covering cardiovascular prostheses according to claim 27 further comprising  
varying pumping capacity for adjusting the size of occurring shear forces.